

Notice of Allowability

Application No.

09/991,448

Examiner

Kathleen M Kerr

Applicant(s)

MCDANIEL, ROBERT

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 4/16/04.
2. ☒ The allowed claim(s) is/are 6, 12, 16, 21 and 22.
3. ☐ The drawings filed on _____ are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.


THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____


Kathleen M Kerr
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DETAILED ACTION

Application Status

1. In response to the previous Office action, a non-Final rejection (mailed on October 22, 2003), Applicants filed a response and amendment received on January 23, 2004. Said amendment cancelled Claims 1, 2, 5, 8, 9, and 18-20, amended Claims 3, 4, 6, 7, 10, 11, and 13, and added new Claims 21 and 22. Thus, Claims 3, 4, 6, 7, 10, 11-17, and 21-22 are pending in the instant Office action and will be examined herein.

Priority

2. The continuity data as corrected in the amendment to the specification on January 23, 2004 correctly cites the priority claims of the instant application.

Compliance with the Sequence Rules

3. As noted by Applicants, a sequence listing in paper copy and computer readable form has been received in conjunction with the instant application (March 19, 2002). The instant application does comply with the sequence rules.

Withdrawn - Objections to the Specification

4. Previous objection to the specification because the title is not descriptive is withdrawn by virtue of Applicants' amendment to the title.

5. Previous objection to the Abstract for not completely describing the disclosed subject matter is withdrawn by virtue of Applicant's amendment.

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6. Previous objection to the specification for lacking complete and correct continuity data in the first paragraph is withdrawn by virtue of Applicant's amendment.

7. Previous objection to the specification for lacking updated information and/or being confusing or incomplete is withdrawn by virtue of Applicants' amendment.

Withdrawn - Objections to the Claims

8. Previous objection to Claim 1 for a misspelling is withdrawn by virtue of Applicant's cancellation of said claim.

Withdrawn - Claim Rejections - 35 U.S.C. § 112

9. Previous rejection of Claims 1-4 and 6-11 under 35 U.S.C. § 112, second paragraph, for the term "P450 monooxygenase" is withdrawn by virtue of Applicants' amendment deleting said term in the claims.

10. Previous rejection of Claims 1-11 under 35 U.S.C. § 112, second paragraph, as being indefinite for lacking method steps is withdrawn by virtue of Applicant's cancellation and amendment to the claims.

11. Previous rejection of Claims 6-7 under 35 U.S.C. § 112, second paragraph, as being indefinite for the terms "a 6-deoxyerythronolide B synthase" and "a 8,8a-deoxyoleandolide synthase" is withdrawn by virtue of Applicant's amendment indicating that the particular DEBS and oleandolide synthase well-known in the art are indicated.

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12. Previous rejection of Claims 12-17 under 35 U.S.C. § 112, second paragraph, as being indefinite for the abbreviation “DEBS” is withdrawn by virtue of Applicant’s amendment.

13. Previous rejection of Claims 11, 13, 15, and 17 under 35 U.S.C. § 112, second paragraph, as being indefinite for their confusing dependence is withdrawn by virtue of Applicant’s amendment.

14. Previous rejection of Claims 1-11, 13, 15, and 17 under 35 U.S.C. § 112, first paragraph, scope of enablement, for using any host cell to introduce groups into any position of any polyketide is withdrawn by virtue of Applicant’s amendment and the Examiner’s amendment below limiting the scope the that which was demonstrated in the examples.

Withdrawn - Claim Rejections - 35 U.S.C. § 102

15. Previous rejection of Claims 1-4 and 6-17 under 35 U.S.C. § 102(e) as being anticipated by Betlach *et al.* is withdrawn by virtue of Applicant’s amendment requiring OleP be used.

16. Previous rejection of Claims 1-4 and 6, 8, and 10 under 35 U.S.C. § 102(a) as being anticipated by Shah *et al.* is withdrawn by virtue of Applicant’s amendment requiring OleP be used.

Withdrawn - Claim Rejections - 35 U.S.C. § 103

17. Previous rejection of Claim 5 under 35 U.S.C. § 103(a) as being unpatentable over Betlach *et al.* (USPN 6,251,636) in view of Rodriguez *et al.* is withdrawn by virtue of Applicant’s amendment. Since the pending claims, as amended by Applicant and by the

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Examiner below, would not be granted priority to the continuation-in-part parent application (clear support for the claimed species of method cannot be found in USPN 6,251,636), Betlach *et al.* would be available as prior art for the purposes of making a rejection, similar to the one withdrawn here, against the pending claims. Thus, the Examiner telephoned Applicant and requested the filing of a statement that the instant invention was owned by the same person as USPN 6,251,636 at the time of its invention (see M.P.E.P. § 706.02(l)(1) and § 706.02(l)(2)). Said communication was filed on April 16, 2004. Thus, Betlach *et al.* is not available as prior art; and Rodriguez *et al.* alone is insufficient to render obvious the pending claims.

EXAMINER'S AMENDMENT

18. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 C.F.R. § 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Carolyn Favorito on April 16, 2004.

Amendments to the Claims

19. The claims have been amended as follows:

- a) Cancel Claims 3, 4, 7, 10, 11, 13-15, and 17.
- b) Amend Claims 6, 12, 16, 21, and 22 (all pending claims) as follows:

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---6. The method of Claim 21, wherein said polyketide is produced by 6-deoxyerythronolide B synthase (DEBS).

12. The method of Claim 21, wherein said host cell is a *Streptomyces* host cell other than *Streptomyces antibioticus*.

16. The method of Claim 12, wherein said host cell is *S. lividans*.

21. A method for introducing two hydroxyl groups or an epoxide into an erythromycin polyketide, which method comprises:

transforming a recombinant nucleic acid sequence encoding OleP into a *Streptomyces* host cell that expresses recombinant nucleic acid sequence encoding an erythromycin polyketide synthase (PKS);

wherein said OleP is not naturally expressed by the host cell;

wherein two hydroxyl groups are introduced at carbons 8 and 8a or wherein an epoxide is introduced at carbons 8 and 8a; and

wherein an erythromycin polyketide is produced.

22. The method of Claim 21, wherein the polyketide is 8,8a-dihydroxy-6-deoxyerythronolide B.---

Reasons for Allowance

20. The following is an examiner's statement of reasons for allowance:

A gene encoding OleP, as used in the claimed invention, is a gene encoding a particular protein with an exact sequence from the oleandolide polyketide synthase (OlePKS) and is indicated to be a P₄₅₀ monooxygenase (see pages 7, 8, and 13 of instant specification). The instant inventor transformed a gene encoding OleP into a host cell, *S. lividans*, expressing heterologous 6-deoxyerythronolide B synthase (DEBS) (see page 8 of specification and Ziermann *et al.* referenced therein) and produced 8,8a-dihydroxy-6-deoxyerythronolide B as confirmed by mass spectrometry and NMR data (see compound 6 in Figure 2 and pages 9-10). Both the epoxide and the characterized dihydro compounds are well-known intermediates in P₄₅₀ monooxygenase reactions. *Streptomyces* are well-known producers of polyketides, and several *Streptomyces* species have been shown to be able to produce erythromycins when transformed with DEBS genes. Thus, the limited breadth of the claimed invention is enabled by the specification. The claims are clear, are useful in the production of dihydro erythromycin analogs, and are free of the prior art as noted in the withdrawal of the rejection under 35 U.S.C. § 103(a) above.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (571) 272-0931.

The examiner can normally be reached on Monday through Friday, from 9:00am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Kathleen M Kerr
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April 18, 2004